

Amendments to the Specification:

Please replace the paragraph (or section) beginning at page 3, line 18, with the following redlined paragraph (or section):

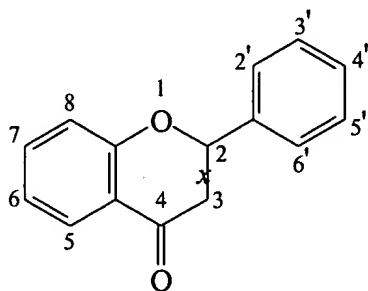
Within other aspects, methods for enhancing chloride transport in epithelial cells may comprise contacting epithelial cells with a compound selected from the group consisting of ~~resveratrol~~resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid. Such compounds may further be used in combination with a flavone or isoflavone as provided above.

Please replace the paragraph (or section) beginning at page 4, line 1, with the following redlined paragraph (or section):

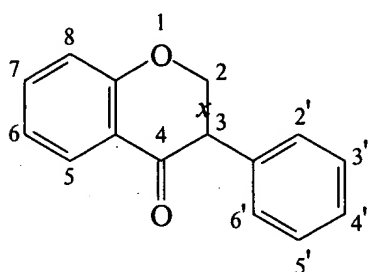
Within other aspects, the present invention provides methods for treating cystic fibrosis in a patient, comprising administering to a patient a compound as described above, wherein the compound is capable of stimulating chloride transport. Within certain embodiments, the compound is genistein, quercetin, apigenin, kaempferol, biochanin A, flavanone, flavone, dihydroxyflavone, trimethoxy-apigenin, apigenin 7-O-neohesperidoside, fisetin, rutin, daidzein or prunetin. Within other embodiments, the compound is ~~resveratrol~~resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid. Such compounds may be administered alone or in combination. Compounds may be administered orally or by inhalation. Within certain embodiments, the compound is combined with a substance that increases expression of a CFTR; and/or a chemical chaperone that increases trafficking of a CFTR to the plasma membrane.

Please replace the paragraph (or section) beginning at page 5, line 4, with the following redlined paragraph (or section):

Within still further aspects, a pharmaceutical composition for treatment of cystic fibrosis may comprise: (a) a polyphenolic compound having the general formula:



or



wherein carbon atoms at positions 2, 3, 5, 6, 7, 8, 2', 3', 4', 5' and 6' are bonded to a moiety independently selected from the group consisting of hydrogen atoms, hydroxyl groups and methoxyl groups, and wherein X is a single bond or a double bond; or a stereoisomer or glycoside derivative of any of the foregoing polyphenolic compounds; (b) a compound selected from the group consisting of ~~resveratrol~~resveratrol, ascorbic acid, ascorbate salts and dehydroascorbic acid; and (c) a physiologically acceptable carrier.

Please replace the paragraph (or section) beginning at page 8, line 14, with the following redlined paragraph (or section):

Figures 13A-13C illustrate the effect of additional representative flavenoids and isoflavenoids on chloride current in epithelial cells. Figure 13A is a graph showing the stimulation of transepithelial chloride currents by ~~resveratrol~~resveratrol (100 μ M), flavanone (100 μ M), flavone (200 μ M), apigenin (20 μ M), apigenin 7-O-neohesperidoside (30 μ M), kaempferol (20 μ M), fisetin (100 μ M), quercetin (30 μ M), rutin (30 μ M), genistein (30 μ M), daidzein (50 μ M), biochanin A (100 μ M) and prunetin (100 μ M) in Calu-3 monolayers.

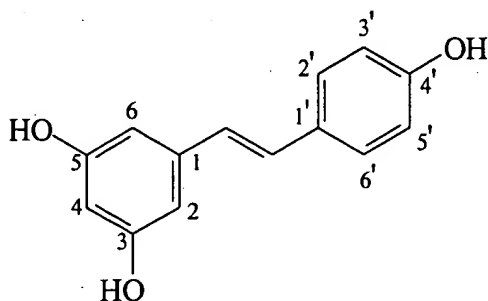
Experiments were performed in the presence of 10 μ M forskolin. Stimulated currents are plotted relative to forskolin stimulated increase (forskolin stimulated currents are 100%). Figure 13B is a recording showing the effect of 7,4'-Dihydroxyflavone on chloride current in unstimulated tissue. This recording shows a dose-dependent stimulation of transepithelial short-circuit current (I_{sc}) across Calu-3 monolayers by 7,4'-Dihydroxyflavone. Increasing concentrations of 7,4'-Dihydroxyflavone (as indicated in μ M) were added to mucosal side and dose-dependently stimulated chloride currents. Currents were recorded with a serosal-to-mucosal chloride gradient at 0 mV and pulses were obtained at 2 mV. Figure 13C is a recording illustrating the effect of trimethoxy-apigenin. This recording shows dose-dependent stimulation of transepithelial short-circuit current (I_{sc}) across Calu-3 monolayers by trimethoxy-apigenin. Increasing concentrations of trimethoxy-apigenin (as indicated in μ M) were added to mucosal side and dose-dependently stimulated chloride currents. Experiment was performed on unstimulated tissue. Currents were recorded with a serosal-to-mucosal chloride gradient at 0 mV and pulses were obtained at 2 mV.

Please replace the paragraph (or section) beginning at page 9, line 6, with the following redlined paragraph (or section):

Figure 14 is a recording illustrating the dose-dependent stimulation of transepithelial short-circuit current (I_{sc}) across Calu-3 monolayers by ~~resveratrol~~resveratrol. Increasing concentrations of ~~resveratrol~~resveratrol (as indicated in μ M) were added to the mucosal perfusion and dose-dependently increased chloride currents. For comparison, currents were further stimulated by serosal addition of 20 μ M forskolin. Stimulated chloride current was completely blocked by addition of the chloride channel blocker DPC (5 mM). Currents were recorded with a serosal-to-mucosal chloride gradient at 0 mV and pulses were obtained at 2 mV.

Please replace the paragraph (or section) beginning at page 18, line 13, with the following redlined paragraph (or section):

As noted above, other polyphenolic compounds may be used within the methods provided herein. For example, trihydroxystilbenes such as ~~resveratrol~~resveratrol (trans-3,5,4'-trihydroxystilbene) may be employed. ~~Resveratrol~~Resveratrol is a polyphenolic compound having the following structure:



Please replace the paragraph (or section) beginning at page 29, line 11, with the following redlined paragraph (or section):

Airway epithelial cells were prestimulated with 10 μ M forskolin. The percent increase in chloride current was then determined following treatment with a series of polyphenolic compounds. Figure 13A summarizes the stimulatory effect of these compounds. On average, chloride currents were further stimulated by ~~resveratrol~~resveratrol (100 μ M) to 135%, by flavanone (100 μ M) to 140%, by flavone (200 μ M) to 128%, by apigenin (20 μ M) to 241%, by apigenin 7-O-neohesperidoside (30 μ M) to 155%, by kaempferol (20 μ M) to 182%, by fisetin (100 μ M) to 108%, by quercetin (30 μ M) to 169%, by rutin (30 μ M) to 149%, by genistein (30 μ M) to 229%, by daidzein (50 μ M) to 162%, by biochanin A (100 μ M) to 139% and by prunetin (100 μ M) to 161%.

Please replace Example 7 beginning at page 30, line 4, with the following redlined Example 7:

Effect of ~~Resveratrol~~Resveratrol on Chloride Currents

This Example illustrates the stimulatory effect of ~~resveratrol~~resveratrol on transepithelial chloride currents.

Unstimulated Calu-3 monolayers were treated with increasing concentrations of ~~resveratrol~~resveratrol. Figure 14 shows the recording generated following the addition of ~~resveratrol~~resveratrol to the mucosal perfusion dose-dependently stimulated transepithelial chloride currents in unstimulated Calu-3 monolayers. For comparison, currents were further stimulated by serosal addition of forskolin. The stimulated chloride current was completely blocked by the Cl⁻ channel blocker DPC. These results indicate that ~~resveratrol~~resveratrol stimulates transepithelial chloride transport.